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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/601,700 | 06/24/2003 | Christopher L. Schardl | 50229-343 | 7548 |

7590 03/31/2006

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| EXAMINER | |
|---|---|
| GEBREYESUS, KAGNEW H | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1652 | |

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/601,700 | SCHARDL ET AL. | |
| | Examiner | Art Unit | |
| | Kagnew H. Gebreyesus | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,14 and 21-25* is/are pending in the application.

4a) Of the above claim(s) *2-13 and 15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,14 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Priority*

Acknowledgement is made for the benefit of priority from U.S. Provisional Application No 60/390,446, filed June 24, 2002.

Applicant's election with traverse dated February 14, 2006 is acknowledged. Claims 1, 14, 21-25 are at issue and are present for examination. Claims 2-13 and 15-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected groups, there being no allowable or linking claims

***Response to Argument:***

Applicants argue "... the claims of Group XVIII (claims 2, 3, 13 and 21-25 in part), which are directed to a polynucleotide sequence consisting of or complementary to ORF8 encoding a γ-type pyridoxal phosphate enzyme within SEQ ID NO: 16, host cells, and method, overlap with the claims of Group VII. The γ-type pyridoxal phosphate enzyme genes of SEQ ID NO: 15 and SEQ ID No: 16 in Groups VII and XVIII share over 95% sequence similarity within their coding sequences. Thus, it would not be an undue burden on the examiner to search these two nearly identical genes".

The argument has been carefully considered but not found persuasive for the following reasons: γ-type pyridoxal phosphate enzymes encompass a variety of enzymes such as O-acetylhomoserine- (thiol) lyase (homocysteine synthase), cystathione γ-synthase, cystathion B-lyase which are γ-type pyridoxal phosphate enzymes that are patentably distinct. Therefore although both Group VII and Group XVIII encode a γ-type pyridoxal phosphate enzymes each sequence is unique and requires a separate search. Each of the inventions requires a separate

patent and non-patent literature search requiring a different text search for each group and thus co-examination of the inventions in groups VII and XVIII would be a serious burden on the examiner. While the search necessary for examination of the various groups may overlap the searches are not coextensive therefore the requirement is still deemed proper and is therefore made FINAL.

### *Claim Objections*

1. Claims 1, 14, 21-25 are objected to because of the following informalities: Claims 1, 14 and 21 comprises non elected subject matter. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 1, 14, 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites, "...wherein the polypeptide encoded by the nucleotide sequence of the variant has insecticidal activity...". However the polypeptides encoded by the open reading frames identified in SEQ ID NO: 15 do not have insecticidal activity per se. Do applicants intend to recite: ' wherein the alkaloid produced by the biosynthetic activity of the polypeptides encoded by the open reading frames in SEQ ID NO: 15 has insecticidal activity? For examination purposes the claim will be read as such.

*Claim Rejections - 35 USC § 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 25 is rejected because although the nucleotide sequence comprising nucleotide residues 6788-8842 of SEQ ID NO: 15 encodes a biosynthetic enzyme involved in the loline alkaloid biosynthesis, the specification does not enable one skilled in the art to practice the method of producing an alkaloid practiced with an expression vector comprising nucleotide residues 6788-8842 of SEQ ID NO: 15 which encodes a single enzyme with γ-type pyridoxal phosphate (PLP) enzyme activity. The specification does not provide enablement for a method whereby a single enzyme can be used to produce any loline alkaloid.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using isolated host cells derived from prokaryotic or a eukaryotic cell line cultured as a unicellular entity in a method of producing specific loline alkaloids, does not reasonably provide enablement for any host cell from any source such as any mammalian cell to produce any type of alkaloid. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988). The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any cell derived from a prokaryotic organism or eukaryotic cell line cultured as a unicellular entity to produce any kind of alkaloid including ergot alkaloids such as clavines, lysergic acid, ergopeptines etc. in addition to loline specific alkaloids. However the specification does not enable any eukaryotic cell such as any mammalian cell to be used in a method of producing any type of alkaloid. The specification provides guidance and examples for a method of using a prokaryotic host cell to produce loline alkaloids using genetically engineered host cells derived from E. coli or more preferred host cells constructed from the Neotyphodium species. However, the specification does not teach a method of producing any alkaloid using any type of host cell.

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed invention is enormous and undue. Such experimentation entails using any host cell from any biological source transformed with gene(s) required in alkaloid production or introducing said genes for alkaloid production by a homologous or heterologous recombination

method. Thus, searching for the specific biological source and the type of alkaloid synthesized is well outside the realm of routine experimentation.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific host cell and the type of alkaloid produced. Without such guidance, the experimentation left to those skilled in the art is undue.

***Conclusion:***

No claims are allowed. However an isolated nucleic acid molecule comprising: a nucleotide sequence consisting of or complementary to nucleotide residues +strand, join 6903-7000, 7063-7114, 7199-7282, 7364-7723, 7810-8364, 8435-8709 (ORF8) of SEQ ID NO: 15 or a nucleotide sequence encoding a variant which hybridizes under high stringency conditions of 0.IXSSC, 0.I%SDS at 65°C to nucleotide residues 6788-8842 of SEQ ID NO: 15 and wherein the encoded polypeptide of said variant has γ-type pyridoxal phosphate (PLP) enzyme activity, vectors and *E.coli* or *Neotyphodium sp.* as host cells comprising ORF 8 will be allowable if re-written with appropriate rectifications.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30 am-5: 30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Achutamurthy ponnathapura can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kagnew Gebreyesus PhD
Claim amendments:

Cancel claims 2-13, 15-20 and 25

Replace claim 1 with:

An isolated nucleic acid molecule comprising: a nucleotide sequence consisting of or complementary to nucleotide residues 6788-8842 of SEQ ID NO: 15 or a nucleotide sequence encoding a variant which hybridizes under high stringency conditions of 0.IXSSC, 0.I%SDS at 65°C to nucleotide residues 6788-8842 of SEQ ID NO: 15 and wherein the encoded polypeptide of said variant has γ-type pyridoxal phosphate (PLP) enzyme activity.

Claim 14:

The isolated nucleic acid of claim 1, wherein nucleotide residues 6788-8842 of SEQ ID NO: 15 encodes *lolC*, a γ-type pyridoxal phosphate (PLP) enzyme involved in loline alkaloid biosynthesis.

21. An expression vector comprising the nucleic acid compound of claim 1.

22. An isolated host cell transformed with an expression vector of claims 21.

23. The host cell according to claim 22 wherein the host cell is a bacterium.

24. The host cell according to claim 23 wherein the host cell is *E. coli*.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kagnew Gebreyesus PhD

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